

# ARS □ ERS □ NASS □ NIFA

## *Policies and Procedures*

**Title:** Protection of Human Subjects

**Number:** 605.1

**Date:** May 13, 2016

**Originating Office:** Office of National Programs

**This Replaces:** 605.1 Dated 6/13/2011

**Distribution:** All REE Employees

REE agencies, and scientists whose work is supported by them, will comply with the Code of Federal Regulations governing protection of human subjects in research. In addition, records from research will be maintained under the Health Insurance Portability and Accountability Act regulations and all clinical trials will be registered with [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

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## 1. Abbreviations

- AD - Area Director
- ARS - Agricultural Research Service
- CD - Center Director
- CFR - Code of Federal Regulations
- EPA - Environmental Protection Agency
- FDA - Food and Drug Administration
- FSIS - Food Safety and Inspection Service
- GRAS - Generally Recognized as Safe
- HHS - Department of Health and Human Services
- HIPAA - Health Insurance Portability and Accountability Act of 1996
- HNRC - Human Nutrition Research Center
- IRB - Institutional Review Board
- OHRP - HHS Office for Human Research Protections
- ONP - Office of National Programs
- RL - Research Leader
- USDA - Department of Agriculture

## 2. Definitions

**2.1 Approved Assurance** is a document stating how the institution conducting research will meet the requirements of the regulations at 7 CFR Part 1c.103 effective January 1, 2008.

**2.2 Certification** is the notice by the institution to ARS that the IRB has approved the research to be conducted.

**2.3 Human Subject** means a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.

**2.4 Minimal Risk** is the risk of harm anticipated in the proposed research that is not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination tests.

## 3. Authorities

7 CFR Part 1c (1-1-2008 Edition or subsequent revisions)

45 CFR 46, Subpart B, Subpart C, Subpart D (7-14-2009 Edition or subsequent revisions)

## 4. Policy

Safeguarding the rights and welfare of human subjects involved in research activities conducted "in house" is ARS' responsibility. When the research activities are conducted with support made available through ARS, either by grant, contract, or cooperative agreement, ARS requires the protection of human subjects be an accepted responsibility of the institution which receives or is accountable to ARS for the support. Such research, as well as "in house" research, must protect

the rights and welfare of the subjects, and must assure each person the right of adequate and appropriate informed consent among other protections. In addition, a safe and healthy environment must be provided to the human subjects if they are restricted during the study. In pursuing this policy, ARS will follow 7 CFR 1c effective January 1, 2008, or subsequent revisions and additional regulations for the protection of human subjects published by HHS in 45 CFR 46 Subparts B, C, and D (EXHIBIT 1) or subsequent revisions, in accordance with the Federal Policy for Protection of Human Subjects. In all research projects covered by this policy, selection of persons or groups for study shall be made without regard to sex, race, color, religion, or national origin, unless these characteristics are factors to be studied. In addition, researchers must complete training in the Responsible Conduct of Research and provide documentation of satisfactory completion to the appropriate line supervisor prior to commencing such research.

## **5. Applicability**

This policy applies to all research conducted “in house” by ARS or supported in whole or in part by grant, contract, or cooperative agreement in which human subjects may be at risk, domestic or foreign including exploratory studies. Personnel affected by this policy include all those involved in the design or conduct of human subject research. This policy also applies to other USDA agencies that conduct research on human subjects; ARS will assist them in adhering to this policy.

Research activities in which the only involvement of human subjects will be in categories as stated in 7 CFR 1c 101(b) are exempt from this policy. These include research involving:

- Educational practices or educational tests.
- Surveys or interview procedures.
- Observation of public behavior.
- Collection of existing data, documents, and records.
- Public benefit or service programs  
Unless information obtained is recorded in such a manner that individuals can be identified or disclosure of responses could result in risk or damage to the individual.
- Taste and food quality evaluation and consumer acceptance studies if wholesome foods without additives are consumed, or if a food is consumed that contains a food ingredient at or below the level found to be safe by the FDA, EPA, or FSIS.

The exempt policy does not apply to taste tests and quality evaluation studies if:

- A food additive is being tested and the test chemical is not:
  - On the FDA’s GRAS list.
  - A permitted food additive as tested.
  - Normally found in food at concentrations being tested.
- Pesticide or other chemical residue is present and the acceptable level has not been established by FDA, EPA, or FSIS.

## **6. Review and Approval**

**IRB.** Except for categories of research specifically exempt, all research, development, or related activities conducted or supported by ARS involving human subjects will be reviewed by an appropriate IRB constituted in accordance with an institution's Federal Wide Assurance

determined in accordance with 7 CFR 1c. This review shall determine that the rights and welfare of the subjects involved are adequately protected and that informed consent is to be obtained by methods that are adequate and appropriate, embodying all the elements of informed consent contained in 7 CFR 1c.116-117.

All investigators, whether ARS scientists or not, supported by Federal funds must submit required protocols to the appropriate IRB. All USDA locations that conduct human subjects research are required to designate one or more IRBs from an organization with an approved Federal Wide Assurance pursuant to the conditions described in 7 CFR 1c.

In addition, the IRB must establish a schedule for continuing review of the activity. Review must be conducted at least annually.

## **7. Procedures – In-House Studies**

### **ARS Scientists who are investigators on a project:**

- Complete training as required by the IRB in the responsible conduct of research plus research involving human subjects and provide certification of completion to line supervisor. NIH provides on-line training at <http://phrp.nihtraining.com/users/login.php> as one example of acceptable training.
- Prepare original and the required number of copies of proposed study.
- Submit a copy of proposed study to CD (or RL and AD if not in a Center) for approval.
- Maintain records for at least three years after completion of research (which includes analysis of data). Assure that HIPAA requirements are met for secure holding of records.
- Provide access to research subjects about their health information if requested. This does not apply to research information on subjects.
- Register the study at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) or other registry prior to commencing research (see Section 10 below).
- Collaborative studies with researchers at other institutions will follow rules established by the principal investigator's home institution.

### **RL**

- At locations other than human nutrition research centers, assure that scientist follows all required procedures related to training, IRB approval, registration of clinical trials, and maintenance of secured records according to HIPAA requirements.
- Provide AD with appropriate documentation.

## **CD**

- Assure that the Center has an active agreement with an institution having a Federal Wide Assurance and whose IRB will review protocols for research with human subjects.
- Assure that all those involved in human subject research have completed required training in the responsible conduct of research.

## **AD**

- Assure that an investigator not located in an HNRC receives training in the responsible conduct of research and is certified as completing that prior to beginning research involving human subjects.
- Assure that the scientist not located in an HNRC has access to an IRB from an institution with a Federal Wide Assurance. This may include university or commercial IRB's.
- Assure that human studies not conducted in an HNRC are registered at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) or another registry prior to initiation of the research.
- Assure that records of IRB activities related to work not conducted at HNRC's are held for at least 3 years after completion of the research.
- Maintain records on numbers of projects with IRB approval submitted from HNRC's for at least 3 years after completion of the research.

## **8. Procedures – Non-ARS**

- For collaborative studies in which the principal investigator is not at an ARS facility but provides humans samples to ARS scientists, the home institution policy will be followed; it is the responsibility of the ARS scientist to assure that those rules cover all issues in this document.
- For research conducted with support made available by ARS, but not conducted by ARS scientists, the cooperating institution's policy on conduct of human studies will apply. Specific responsibilities follow:

### **Research Investigator**

- Submit a copy of proposed study to CD, if required by local policy.
- Submit required number of copies of approved proposal for review to an IRB constituted in accordance with an approved Federal Wide Assurance on file with HHS.
- Retain records of informed consent, following institutional policy, for at least 3 years after completion of the research.

- Maintain research records for at least 3 years after completion of research.
- Assure that HIPAA requirements are met for secure holding of records, plus provide access to research subjects about their health information if requested.
- Register the study, or have an institutional official register, at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) or other registry prior to commencing research as designated in Section 10 below.

## **CD**

- Assure that records of IRB activities be held for at least 3 years after completion of research.
- Provide an annual report of the number of projects conducting research on human subjects to the Area Office.

## **AD**

- Maintain records on numbers of projects with IRB approval submitted from HNRC's for at least 3 years after completion of the research.

## **9. Deviations from Approved Protocols**

Whether intentional or accidental, if a deviation from an approved protocol occurs or any research on human subjects is done without an approved protocol, the principal investigator must report that to the chair of the relevant IRB, the local biosafety officer, physician with study oversight of the CD, AD, and responsible institutional official within guidelines from HHS/OHRP. The CD, or his/her designee, will assure compliance with this. The AD will seek advice from ONP on the seriousness of the deviation and whether a formal investigation by ARS is required.

## **10. Registration of Clinical Trials**

Clinical Trials are defined as studies in human beings that follow a pre-defined protocol. Most nutritional studies on humans fall under this definition; while all interventions, including any feeding study, must be registered, observational studies are not required to be registered but it is strongly encouraged that they be registered. Therefore, where appropriate, it is the responsibility of the investigator to register the trial with [ClinicalTrials.gov](http://ClinicalTrials.gov) prior to commencing work. Generally, an organization account will be used to register all the trials conducted at a location, whether an ARS facility or a non-ARS facility. Therefore, it is the responsibility of the CD to ensure that an organization account is maintained for each location. If research is done by a single investigator outside of a HNRC, an individual account should be used to register that trial.

Approved by:

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CHAVONDA JACOBS-YOUNG  
Administrator, ARS

Exhibit 1: 7 CFR 1c, and 45 CFR 46 Subparts B, C, and D



**7 CFR 1c**  
**Revised January 1, 2008**  
**and**  
**45 CFR 46, Subparts B, C and D**  
**Revised July 14, 2009**

Protection of Human Subjects

Reprinted From the Code of Federal Regulations

## 7 CFR Part 1c - PROTECTION OF HUMAN SUBJECTS

### § 1c.101 To what does this policy apply?

(a) Except as provided in paragraph (b) of this section, this policy applies to all research involving human subjects conducted, supported or otherwise subject to regulation by any Federal department or agency which takes appropriate administrative action to make the policy applicable to such research. This includes research conducted by Federal civilian employees or military personnel, except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint. It also includes research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States.

- (1) Research that is conducted or supported by a Federal department or agency, whether or not it is regulated as defined in § 1c.102(e), must comply with all sections of this policy.
- (2) Research that is neither conducted nor supported by a Federal department or agency but is subject to regulation as defined in § 1c.102(e) must be reviewed and approved, in compliance with §§ 1c.101, 1c.102, and 1c.107 through 1c.117 of this policy, by an institutional review board (IRB) that operates in accordance with the pertinent requirements of this policy.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

- (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
    - (i) Research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
  - (2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
    - (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
    - (ii) Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.
  - (3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
    - (i) The human subjects are elected or appointed public officials or candidates for public office; or
    - (ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
  - (4) Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.
  - (5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:
    - (i) Public benefit or service programs;
    - (ii) Procedures for obtaining benefits or services under those programs;
    - (iii) Possible changes in or alternatives to those programs or procedures; or
    - (iv) Possible changes in methods or levels of payment for benefits or services under those programs.
  - (6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
- (c) Department or agency heads retain final judgment as to whether a particular activity is covered by this policy.

(d) Department or agency heads may require that specific research activities or classes of research activities conducted, supported,

or otherwise subject to regulation by the department or agency but not otherwise covered by this policy, comply with some or all of the requirements of this policy.

- (e) Compliance with this policy requires compliance with pertinent Federal laws or regulations which provide additional protections for human subjects.
- (f) This policy does not affect any state or local laws or regulations which may otherwise be applicable and which provide additional protections for human subjects.
- (g) This policy does not affect any foreign laws or regulations which may otherwise be applicable and which provide additional protections to human subjects of research.
- (h) When research covered by this policy takes place in foreign countries, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. [An example is a foreign institution which complies with guidelines consistent with the World Medical Assembly Declaration (Declaration of Helsinki amended 1989) issued either by sovereign states or by an organization whose function for the protection of human research subjects is internationally recognized.] In these circumstances, if a department or agency head determines that the procedures prescribed by the institution afford protections that are at least equivalent to those provided in this policy, the department or agency head may approve the substitution of the foreign procedures in lieu of the procedural requirements provided in this policy. Except when otherwise required by statute, Executive Order, or the department or agency head, notices of these actions as they occur will be published in the Federal Register or will be otherwise published as provided in department or agency procedures.
- (i) Unless otherwise required by law, department or agency heads may waive the applicability of some or all of the provisions of this policy to specific research activities or classes of research activities otherwise covered by this policy. Except when otherwise required by statute or Executive Order, the department or agency head shall forward advance notices of these actions to the Office for Human Research Protections, Department of Health and Human Services (HHS), or any successor office, and shall also publish them in the Federal Register or in such other manner as provided in department or agency procedures.

#### § 1c.102 Definitions.

- (a) Department or agency head means the head of any Federal department or agency and any other officer or employee of any department or agency to whom authority has been delegated.
- (b) Institution means any public or private entity or agency (including Federal, state, and other agencies).
- (c) Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.
- (d) Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.
- (e) Research subject to regulation, and similar terms are intended to encompass those research activities for which a Federal department or agency has specific responsibility for regulating as a research activity, (for example, Investigational New Drug requirements administered by the Food and Drug Administration). It does not include research activities which are incidentally regulated by a Federal department or agency solely as part of the department's or agency's broader responsibility to regulate certain types of activities whether research or non-research in nature (for example, Wage and Hour requirements administered by the Department of Labor).
- (f) Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:
  - (1) Data through intervention or interaction with the individual, or
  - (2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject. "Private information" includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been

provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.

- (g) IRB means an institutional review board established in accord with and for the purposes expressed in this policy.
- (h) IRB approval means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.
- (i) Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- (j) Certification means the official notification by the institution to the supporting department or agency, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

**§ 1c.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.**

- (a) Each institution engaged in research which is covered by this policy and which is conducted or supported by a Federal department or agency shall provide written assurance satisfactory to the department or agency head that it will comply with the requirements set forth in this policy. In lieu of requiring submission of an assurance, individual department or agency heads shall accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections, HHS, or any successor office, and approved for Federal wide use by that office. When the existence of an HHS-approved assurance is accepted in lieu of requiring submission of an assurance, reports (except certification) required by this policy to be made to department and agency heads shall also be made to the Office for Human Research Protections, HHS, or any successor office.
- (b) Departments and agencies will conduct or support research covered by this policy only if the institution has an assurance approved as provided in this section, and only if the institution has certified to the department or agency head that the research has been reviewed and approved by an IRB provided for in the assurance, and will be subject to continuing review by the IRB. Assurances applicable to federally supported or conducted research shall at a minimum include:
  - (1) A statement of principles governing the institution in the discharge of its responsibilities for protecting the rights and welfare of human subjects of research conducted at or sponsored by the institution, regardless of whether the research is subject to Federal regulation. This may include an appropriate existing code, declaration, or statement of ethical principles, or a statement formulated by the institution itself. This requirement does not preempt provisions of this policy applicable to department- or agency-supported or regulated research and need not be applicable to any research exempted or waived under § 1c.101 (b) or (i).
  - (2) Designation of one or more IRBs established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IRB's review and recordkeeping duties.
  - (3) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the department or agency head, unless in accord with § 1c.103(a) of this policy, the existence of an HHS-approved assurance is accepted. In this case, change in IRB membership shall be reported to the Office for Human Research Protections, HHS, or any successor office.
  - (4) Written procedures which the IRB will follow (i) for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and (iii) for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.
  - (5) Written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval.

- (c) The assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the department or agency head prescribes.
- (d) The department or agency head will evaluate all assurances submitted in accordance with this policy through such officers and employees of the department or agency and such experts or consultants engaged for this purpose as the department or agency head determines to be appropriate. The department or agency head's evaluation will take into consideration the adequacy of the proposed IRB in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.
- (e) On the basis of this evaluation, the department or agency head may approve or disapprove the assurance, or enter into negotiations to develop an approvable one. The department or agency head may limit the period during which any particular approved assurance or class of approved assurances shall remain effective or otherwise condition or restrict approval.
- (f) Certification is required when the research is supported by a Federal department or agency and not otherwise exempted or waived under § 1c.101 (b) or (i). An institution with an approved assurance shall certify that each application or proposal for research covered by the assurance and by § 1c.103 of this Policy has been reviewed and approved by the IRB. Such certification must be submitted with the application or proposal or by such later date as may be prescribed by the department or agency to which the application or proposal is submitted. Under no condition shall research covered by § 1c.103 of the Policy be supported prior to receipt of the certification that the research has been reviewed and approved by the IRB. Institutions without an approved assurance covering the research shall certify within 30 days after receipt of a request for such a certification from the department or agency, that the application or proposal has been approved by the IRB. If the certification is not submitted within these time limits, the application or proposal may be returned to the institution.

#### § 1c.116 General requirements for informed consent.

Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

- (a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:
  - (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
  - (2) A description of any reasonably foreseeable risks or discomforts to the subject;
  - (3) A description of any benefits to the subject or to others which may reasonably be expected from the research;
  - (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
  - (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
  - (6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
  - (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and
  - (8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

- (b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:
  - (1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
  - (2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
  - (3) Any additional costs to the subject that may result from participation in the research;
  - (4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
  - (5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
  - (6) The approximate number of subjects involved in the study.
- (c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:
  - (1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) Public benefit of service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
  - (2) The research could not practicably be carried out without the waiver or alteration.
- (d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:
  - (1) The research involves no more than minimal risk to the subjects;
  - (2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
  - (3) The research could not practicably be carried out without the waiver or alteration; and
  - (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- (e) The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.
- (f) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, state, or local law.

#### § 1c.117 Documentation of informed consent.

- (a) Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.
- (b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:
  - (1) A written consent document that embodies the elements of informed consent required by § 1c.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or
  - (2) A short form written consent document stating that the elements of informed consent required by § 1c.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the

short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

**TITLE 45 PUBLIC WELFARE**  
**PART 46 PROTECTION OF HUMAN SUBJECTS**  
**SUBPART B**

**§46.201 To what do these regulations apply?**

- (a) Except as provided in paragraph (b) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Department of Health and Human Services (DHHS). This includes all research conducted in DHHS facilities by any person and all research conducted in any facility by DHHS employees.
- (b) The exemptions at §46.101(b)(1) through (6) are applicable to this subpart.
- (c) The provisions of §46.101(c) through (i) are applicable to this subpart. Reference to State or local laws in this subpart and in §46.101(f) is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments.
- (d) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

**§46.202 Definitions.**

The definitions in §46.102 shall be applicable to this subpart as well. In addition, as used in this subpart:

- (a) Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.
- (b) Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.
- (c) Fetus means the product of conception from implantation until delivery.
- (d) Neonate means a newborn.
- (e) Nonviable neonate means a neonate after delivery that, although living, is not viable.
- (f) Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.
- (g) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.
- (h) Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the FEDERAL REGISTER guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

#### §46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart and the other subparts of this part.

#### §46.204 Research involving pregnant women or fetuses.

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

- (a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- (b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- (c) Any risk is the least possible for achieving the objectives of the research;
- (d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part;
- (e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- (f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- (g) For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
- (h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- (i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- (j) Individuals engaged in the research will have no part in determining the viability of a neonate.

#### §46.205 Research involving neonates.

(a) Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

- (1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- (2) Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- (3) Individuals engaged in the research will have no part in determining the viability of a neonate.
- (4) The requirements of paragraph (b) or (c) of this section have been met as applicable.
- (b) Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:



(1) The IRB determines that:

(i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

(ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

(2) The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) Nonviable neonates. After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

(1) Vital functions of the neonate will not be artificially maintained;

(2) The research will not terminate the heartbeat or respiration of the neonate;

(3) There will be no added risk to the neonate resulting from the research;

(4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

(d) Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of this part.

§46.206 Research involving, after delivery, the placenta, the dead fetus or fetal material.

(a) Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, state, or local laws and regulations regarding such activities.

(b) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

§46.207 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if:

(a) The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and

(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:

(1) That the research in fact satisfies the conditions of §46.204, as applicable; or

(2) The following:

- (i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
- (ii) The research will be conducted in accord with sound ethical principles; and
- (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

### **Subpart C**

#### **Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects** **§46.301 Applicability.**

- (a) The regulations in this subpart are applicable to all biomedical and behavioral research conducted or supported by the Department of Health and Human Services involving prisoners as subjects.
- (b) Nothing in this subpart shall be construed as indicating that compliance with the procedures set forth herein will authorize research involving prisoners as subjects, to the extent such research is limited or barred by applicable State or local law.
- (c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

#### **§46.302 Purpose.**

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

#### **§46.303 Definitions.**

As used in this subpart:

- (a) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.
- (b) DHHS means the Department of Health and Human Services.
- (c) Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.
- (d) Minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

#### **§46.304 Composition of Institutional Review Boards where prisoners are involved.**

In addition to satisfying the requirements in §46.107 of this part, an Institutional Review Board, carrying out responsibilities under this part with respect to research covered by this subpart, shall also meet the following specific requirements:

- (a) A majority of the Board (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the Board.
- (b) At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

#### **§46.305 Additional duties of the Institutional Review Boards where prisoners are involved.**

- (a) In addition to all other responsibilities prescribed for Institutional Review Boards under this part, the Board shall review research covered by this subpart and approve such research only if it finds that:
  - (1) The research under review represents one of the categories of research permissible under §46.306(a)(2);

- (2) Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
- (3) The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;
- (4) Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
- (5) The information is presented in language which is understandable to the subject population;
- (6) Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- (7) Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.
- (b) The Board shall carry out such other duties as may be assigned by the Secretary.
- (c) The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

#### §46.306 Permitted research involving prisoners.

- (a) Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:
  - (1) The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under §46.305 of this subpart; and
  - (2) In the judgment of the Secretary the proposed research involves solely the following:
    - (j) Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    - (ii) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    - (iii) Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his intent to approve such research; or
    - (iv) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of the intent to approve such research.
- (b) Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

#### **Subpart D**

#### **Additional Protections for Children Involved as Subjects in Research**

#### **§46.401 To what do these regulations apply?**

- (a) This subpart applies to all research involving children as subjects, conducted or supported by the Department of Health and Human Services.
- (1) This includes research conducted by Department employees, except that each head of an Operating Division of the Department may adopt such nonsubstantive, procedural modifications as may be appropriate from an administrative standpoint.
- (2) It also includes research conducted or supported by the Department of Health and Human Services outside the United States, but in appropriate circumstances, the Secretary may, under paragraph (e) of §46.101 of subpart A, waive the applicability of some or all of the requirements of these regulations for research of this type.
- (b) Exemptions at §46.101(b)(1) and (b)(3) through (b)(6) are applicable to this subpart. The exemption at §46.101(b)(2) regarding educational tests is also applicable to this subpart. However, the exemption at §46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research covered by this subpart, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.
- (c) The exceptions, additions, and provisions for waiver as they appear in paragraphs (c) through (i) of §46.101 of subpart A are applicable to this subpart.

#### §46.402 Definitions.

The definitions in §46.102 of subpart A shall be applicable to this subpart as well. In addition, as used in this subpart:

- (a) Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
- (b) Assent means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- (c) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in research.
- (d) Parent means a child's biological or adoptive parent.
- (e) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

#### §46.403 IRB duties.

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart.

#### §46.404 Research not involving greater than minimal risk.

HHS will conduct or fund research in which the IRB finds that no greater than minimal risk to children is presented, only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

#### §46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that:

- (a) The risk is justified by the anticipated benefit to the subjects;
- (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

- (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §46.408.

§46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.

HHS will conduct or fund research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:

- (a) The risk represents a minor increase over minimal risk;
- (b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in §46.408.

§46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

HHS will conduct or fund research that the IRB does not believe meets the requirements of §46.404, §46.405, or §46.406 only if:

- (a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- (b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
  - (1) that the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or (2) the following:
    - (i) the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - (ii) the research will be conducted in accordance with sound ethical principles;
    - (iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in §46.408.

§46.408 Requirements for permission by parents or guardians and for assent by children.

- (a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.
- (b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by

§§46.406 and 46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

- (c) In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.
- (d) Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117 of subpart A.
- (e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

#### §46.409 Wards.

- (a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such research is:
  - (1) Related to their status as wards; or
  - (2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
- (b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.